

IN THE UNITED STATES PATENT AND TRADEMARK OFFICE

In re Patent Application of

Antoni SANTAMARIA

Atty. Ref.: 613-97; Confirmation No.

Appl. No. 10/537,989

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Filed:

Examiner: Unknown

For: ANHYDROUS CRYSTALLINE FORM OF VALACYCLOVIR HYDROCHLORIDE

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Commissioner for Patents
P.O. Box 1450
Alexandria, VA 22313-1450

Sir:

DECLARATION OF ANTONI SANTAMARIA

I, Antoni Santamaria, hereby declare and state as follows:

That I am a Spanish citizen residing at Viladordis 74, E-08240 Manresa, Spain; that I have been listed as the sole inventor in respect of International Patent Application PCT/EP2003/01591 filed 9 December 2003 and published as WO 2004/052892 A1 of which the above-identified U.S. patent application is a national stage entry of WO 2004/052892 A1.


That I have reviewed claims 1-15 of the above-identified U.S. patent application as reproduced in Appendix A attached hereto, and do not believe that I am an inventor of any of the subject matter defined by these claims. Designating me as an inventor occurred without deceptive intention on my part.

I declare further that all statements made herein of my own knowledge are true and that all statements made on information and belief are believed to be true; and further that these statements were made with the knowledge that willful false statements and the like so made are punishable by fine or imprisonment, or both, under Section 1001 of Title 18 of the United States

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Code and that such willful false statements may jeopardize the validity of the application or any patent issuing thereon.

Date: October 20, 2005



Antoni Santamaria

Claims

1. Valacyclovir hydrochloride in anhydrous crystalline form having substantially the following d-spacing pattern (in angstroms):

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d-spacing
6.76
9.36
11.54
13.98
15.45
15.75
17.12
19.10
21.39
23.02
24.23
26.41
27.46
28.06

2. Valacyclovir hydrochloride in anhydrous crystalline form as claimed in claim 1 having substantially the X-ray diffraction pattern of Figure 2.

3. Valacyclovir hydrochloride in anhydrous crystalline form having substantially the characteristic infrared peaks

IR (cm⁻¹): 1686.42, 1572.60, 1533.52.

4. Valacyclovir hydrochloride in anhydrous crystalline form as claimed in claim 3 having substantially the characteristic infrared peaks

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IR (cm⁻¹): 3377.99, 3285.87, 3197.62, 2930.92, 1749.72, 1686.42, 1631.12, 1607.17, 1572.60, 1533.52, 1476.48, 1364.98, 1298.63, 1258.79, 1248.27, 1225.22, 1132.81, 1097.06, 778.37, 759.33.

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5. Valacyclovir hydrochloride in anhydrous crystalline form as claimed in claim 3 having substantially the infra-red absorption spectrum of Figure 1.

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6. A pharmaceutical composition comprising a valacyclovir hydrochloride form as claimed in claim 1 to 5 along with one or more pharmaceutical carriers/excipients.

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7. Valacyclovir hydrochloride in anhydrous crystalline form as claimed in claim 1 to 5 for use in medicine.

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8. Use of valacyclovir hydrochloride in anhydrous crystalline form as claimed in claim 1 to 5 in the manufacture of a medicament for use as an antiviral agent.

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9. A process for the preparation of valacyclovir hydrochloride in anhydrous crystalline form as claimed in claim 1 to 5 comprising;

1) mixing valacyclovir hydrochloride hydrate with a substantially pure C₁₋₆ lower alcohol solvent and heating the resulting suspension;

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2) evaporating the solvent under reduced pressure and isolating the resulting solid.

10. The process of claim 9 wherein said solvent is ethanol.

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11. The process of claim 9 or 10 wherein the suspension is heated at between 50 to 70°C for at least 12 hours.

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12. The process of claim 11 wherein the suspension is heated at 60°C for 20-21 hours.

5 13. A process for the preparation of valacyclovir hydrochloride in anhydrous crystalline form as claimed in claim 1 to 5 comprising;

1) mixing valacyclovir hydrochloride hydrate with a substantially pure C₁₋₆ lower alcohol solvent and adding the resulting suspension to substantially pure refluxing lower alcohol;

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2) distilling off the solvent to form a suspension and maintaining the same at room temperature for at least 8 hours; and

3) isolating the resulting solid.

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14. The process of claim 13 wherein the solvent and refluxing lower alcohol are ethanol.

20 15. The process of claim 13 or 14 wherein approximately one third of the solvent is distilled off to form said suspension.